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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,161	09/30/2005	Charles Tellier	0512-1258	3550

466 7590 12/31/2008

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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1639	
MAIL DATE	DELIVERY MODE
12/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,161	TELLIER ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7-15 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7-15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner on the present case has changed. See contact information below. Responsive to communications entered 1/9/2008 Claims 1,2,4,7-15,19 are pending. Claims 1,2,4,7-15,19 are under consideration.

Election/Restrictions

Applicant's election of a 5' phosphate nucleic acid with a poly G spacer for the species of biopolymer in the reply filed on 1/9/2008 is acknowledged. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

The present application filed was 9/30/2005 and is a 371 of PCT/FR03/02318 filed 07/22/2003.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to French application 02/09456 (referred to as '456) filed 07/25/2002. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Applicant has perfected priority to '456 by filing a certified and verified English translation of '456 on 1/9/2008.

Withdrawn Objection(s) and/or Rejection(s)

The rejection of claims 1 and 13 and by dependency, claims 2-12 and 14-16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicant's amendments.

The rejection of claim 16 under 35 USC 102(e) as being unpatentable over Stahler et al, (US Patent 7,097,974) is hereby withdrawn in view of applicant's cancellation of claim 16.

The rejection of claims 1, 4, 7-15 under 35 U SC. 103(a) as being unpatentable over **Agrawal et al**, (WO 2003/046508 A2) in view of **Petruska, et al**, (Thin Solid Films, 327-329 (1998) 131-135, Elsevier Science) and **Lockhart et al**, (US Patent 5,556,752) is hereby withdrawn in view of applicant's persuasive arguments.

Maintained Claim Rejection(s) - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 7-15, 2 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Agrawal et al**, (WO 2003/046508 A2) in view of **Petruska, et al**, (Thin Solid Films, 327-329 (1998) 131-135, Elsevier Science) and **Lockhart et al**, (US Patent 5,556,752) , and further in view of **Gagna et al**, US Patent 6,936,461 (Date of Patent 30 August 2005)

For claims 1, 4, 7-14, a biochip, comprising a flat solid support having a surface covered with a metal and capable of coordination bonding with a phosphate at least one biopolymer carrying a free phosphate group being immobilized on said surface by ionocovalent bonding between the free phosphate group of the polymer and the metal.

Agrawal et al teach (see paragraph 25) a biomolecule, which can be a nucleic acid, immobilized to a glass solid support substrate (see paragraphs 20 and 80). The biomolecule is covalently/coordinately attached to the substrate (see paragraphs 131 and 132). The solid support can be coated with an organic or inorganic activating material such as zirconia (see paragraphs 42, 144). The activating material is used to help immobilize the biomolecule to the solid support.

The prior art teachings of Agrawal et al differ from the claimed invention as follows:
Agrawal; et al, fail to teach the following:

Agrawal et al, fail to teach a metal, zirconium, is bound to the surface of the solid support by a spacer molecule, octadecylphosphonic acid. Agrawal et al, also fail to teach specifically a zirconium bonding with a phosphate group.

However, the teachings of Petruska, et al, remedies the deficiencies of Agrawal et al, as follows:

Petruska et al, teach (see Scheme 1 and Scheme 2) a biochip wherein the zirconium is bound to the surface of the support by way of a spacer molecule comprising a fatty acid chain, octadecylphosphonic acid (as recited in claims 7 and 8).

Petruska et al, teach (see abstract, introduction, scheme 2) a biochip wherein the spacer molecule (also called a capping molecule) is octadecylphosphonic acid and the metal is zirconium (as recited in claim 10).

Petruska et al, teach (see abstract, and definition of Langmuir monolayer method) a biochip, further comprising a sheet of glass having a surface covered with a monolayer of zirconium octadecylphosphonate (as recited in claim 12).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the device and method of immobilizing a nucleic acid onto a glass solid support that has been covered with zirconia on a biochip as taught by Agrawal et al, with the Langmuir-Blodgett film method (a Langmuir-Blodgett (LB) film is a set of monolayers, or layers of organic material one molecule thick, deposited on a solid substrate. An LB film can consist of a single layer or many) as taught by Petruska et al.

A person of ordinary skill in the art would have been motivated to combine the device of the biochip and the method of making the biochip which has a nucleic acid immobilized onto a glass solid support which has been covered in a layer of zirconia as taught by Agrawal et al, with the Langmuir-Blodgett method as taught by Petruska et al, because the zirconium/phosphate interaction is strong, and the nature of the stepwise procedure employed allows for the easy construction of alternating layer of LB films which results in a procedure that is an extremely convenient way to prepare alternating layer films (see introduction, Petruska, et al).

Petruska et al, teach the use of a metal, zirconium, bound to a spacer molecule. Formation of the Langmuir-Blodgett monolayer to the support is made up of Octadecylphosphonic acid that serves as the spacer molecule attached to zirconium to aid in binding to the support (see scheme 2),

Furthermore, because of the strength of the metal-head group interactions, zirconium phosphate films are extremely stable LB assemblies (see conclusions, Petruska et al).

Finally a person of ordinary skill in the. art would have had a reasonable expectation of success because utilizing the system described by Petruska to more stably immobilize a biopolymer to a solid support is a well-known method in the art. The Langmuir-Blodgett method is well described in the prior art and has robust elements for reliably coordinately bonding a metal to an organic molecule on a solid support.

Agrawal et al, in view of Petruska et al, fail to teach a polyG spacer group between the body of the nucleic acid and the phosphate group.

However Lockhart et al, further remedies the deficiencies of Agrawal et al, and Petruska et al, as follows:

Lockhart et al, teach (see Figures 1B and 1C) a nucleic acid bound to a solid support with a spacer or linker (element 4) attached between the body of one nucleic acid and the attached to the end of another nucleic acid (as recited in claim 4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to further combine and modify the device and method of immobilizing a nucleic acid on a biochip as taught by Agrawal et al, with the Langmuir-Blodgett film method as taught by Petruska et al, with a spacer molecule for attaching a nucleic acid to a glass support (with a metal coating) as taught by Lockhart et al.

A person of ordinary skill in the art would have been motivated to combine and further modify the device of the biochip and the method of making the biochip with the addition of a spacer molecule to further immobilize the nucleic acid to the solid support because (see column 8, lines 58-62; column 10, lines 15-17) addition of the spacer molecule (as taught by Lockhart et al.) permits the oligonucleotides (for example, double-stranded DNA) in the completed member of the library to interact freely with the molecules exposed to the library. Lockhart et al, also the spacer molecule can be used for construction of the libraries in the same manner as photolabile-protected

phosphoramidite activated nucleotides (see column 10, lines 15-17). This will enable better binding and detection of signal after hybridization.

Finally a person of ordinary skill in the art would have had a reasonable expectation of success because utilizing the system described by Lockhart et al., when combined with the teachings of Agrawal et al, and Petruska et al, to more stably immobilize a biopolymer to a solid support is a well-known method in the art. The Langmuir-Blodgett method is well described in the prior art and has robust elements for reliably coordinately bonding a metal to an organic molecule on a solid support.

Agrawal et al, in view of Petruska et al, and Lockhart et al, fail to teach a nucleic acid phosphorylated in the 5' position and polyG spacer group.

However, the teachings of **Gagna et al**, remedies the deficiencies of Agrawal et al, in view of Petruska et al, and Lockhart et al, as follows:

For claims 2, 15 and 19 the biochip according to claim 1, wherein the biopolymer is a nucleic acid phosphorylated in the 5' position; furthermore, the nucleic acid has a polyguanine spacer group between the nucleic acid and the phosphate group Gagna et al, teach (see column 17, line 66, column 23, line 58) a nucleic acid phosphorylated in the 5' position. Each nucleic acid has a tail (which the examiner contends is a linker or spacer) to help immobilize the nucleic acid to the substrate (see column 25, lines 33-37).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine and modify the teachings of a biochip containing a nucleic acid immobilized on a solid support and the method of making the biochip as taught by Agrawal et al., and the method of coating a glass solid support with the metal Zirconium covalently attached to a phosphate group as taught by Petruska et al, and Lockhart et al, with a linker attached to the body of a nucleic acid phosphorylated in the 5' position as taught by Gagna et al.

A person of ordinary skill in the art would have been motivated to combine and modify the teachings of Agrawal et al, in view of Petruska et al, and Lockhart et al, to include the use of a linker attached to the body of a nucleic acid phosphorylated in the 5' position as taught by Gagna et al, because the tail or linker immobilizes the nucleic acid

more firmly to the substrate (see column 25, lines 33-37). Also, by attaching the nucleic acid to the glass surface allows the investigator the ability to characterize nucleic acid/probe interactions (see column 23, lines 24-26).

Finally a person of ordinary skill in the art would have had a reasonable expectation of success because the methods of using modified nucleic acids attached to a solid support as taught by Gagna et al, is well known in the art for use in this manner

Response to Amendment

The declaration filed on 1/9/2008 under 37 CFR 1.131 has been considered but is ineffective to overcome the Agrawal et al and Gagna references because in accordance with MPEP 715.04 I A, all the inventors of the claimed subject matter claimed have not signed the declaration.

Response to Arguments

In the remarks entered 1/9/2008, applicant argues: (i) the declaration filed 1/9/2008 antedates the Agrawal et al and Gagna et al references; (ii) not all elements are taught; (iii) there is a lack of motivation to combine the teachings of Petruska et al and Lockhart et al with Agrawal et al.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

(i) On p 8 of applicant's remarks, applicant appears to contend that the claimed subject matter was reduced to practice by the inventors on 4/30/2001 base upon evidence provided in the "Envelope Soleau" of the 37 CFR 1.131 declaration entered 1/9/2008, which is prior to 11/9/2001, the effective filing date of the Agrawal et al

reference. However, for the reasons set forth above, the 37 CFR 1.131 declaration is deemed ineffective.

On p 9 of applicant's remarks, applicant appears to contend that the claimed subject matter was reduced to practice by the inventors on 4/30/2001 base upon evidence provided in the "Envelope Soleau" of the 37 CFR 1.131 declaration entered 1/9/2008, which is prior to 7/31/2001, the effective filing date of the Gagna reference. However, for the reasons set forth above, the 37 CFR 1.131 declaration is deemed ineffective.

(ii) On p 8, applicant argues that biopolymers are not taught by Petruska et al.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, biopolymers are taught by Agrawal et al, as mentioned in the last office action.

On p 8-9, applicant argues that Lockhart et al do not teach solid support having surface covered by a metal.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.

1986). Here, solid support having surface covered by a metal taught by Petruska et al: see especially scheme 2 step 3.

(ii) On p 9, applicant seems to argue it would not have been obvious for the skilled artisan to apply the teachings of Petruska et al and Lockhart et al to generate a biochip bearing phosphorylated biopolymers linked to a metal surface through ionocovalent bonding.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, biochips taught by Agrawal et al, as mentioned in the last office action.

With regard to ionocovalent bonding, solely to rebut applicant's argument, evidence by Brousseau et al (1994 ACS Symposium Series 561:60-70) indicates phosphosphonates inherently form ionocovalent bonds with tetravalent metals, such as the Zirconium taught by Petruska et al. See Abstract. Absent evidence to the contrary, a 5' phosphate oligonucleotide, such as presented by Gagna et al would exhibit similar bonding properties.

New Claim Rejection(s) – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1,2,4,7-15,19 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The rejection is necessitated by new evidence provided by applicant.

Evidence provided in the Envelope Soleau submitted to the Office on 1/9/2008 on p 2 of the English translation indicates Pascal Janvier and Isa Benitez as inventors, yet Mr. Janvier and Ms. Benitez are *not* listed as inventors of the present application.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571 272 0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1639